UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/451,666	11/30/1999	TOSHIAKI ITO	07898-051001	9360

20985 7590 08/09/2002

FISH & RICHARDSON, PC
4350 LA JOLLA VILLAGE DRIVE
SUITE 500
SAN DIEGO, CA 92122

EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/451,666	ITO ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,9-15 and 23-41* is/are pending in the application.

4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7 and 23-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8 June 2002 has been entered.

2. This action is in response to papers filed 8 June 2002 in Paper No. 30 in which claims 24-28 and 34-36 were amended, claim 21 was canceled and new claims 37-41 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 25 dated 2 January 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Currently claims 6, 7 and 23-41 are under prosecution.

Information Disclosure Statement

3. The reference submitted with the Supplemental Information Disclosure Statement of 22 August 2001 has been reviewed. A 1449 listing the reference was not received.

Specification

4. The amendment filed 8 June 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Newly amended Claims recite "wherein the binding agent is not conjugated to the probe". However, the specification, as originally filed, fails to define or provide any disclosure to support such claim recitation. The specification teaches a preferred binding agent is selected from the group "comprising" poly-l-lysine, carbodiimide and silylation-coating (page 4, last paragraph) but the specification does not teach the "binding agent is not conjugated to the probe". Therefore, newly amendment claims introduce subject matter not described in the specification, as originally filed.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

35 USC § 112: First Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 7, 24 and 37-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To the extent that the claimed composition/or methods are not described in the instant disclosure, Claims 7, 24 and 37-41 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

The recitation "wherein the binding agent is not conjugated to the probe" is added to the newly amended independent claim 24. However, the specification fails to define or provide any disclosure to support such claim recitation. The specification teaches a preferred binding agent is selected from the group "comprising" poly-l-lysine, carbodiimide and silylation-coating (page 4, last paragraph) but the specification does not teach the "binding agent is not conjugated to the probe". Therefore, newly amendment claims introduce subject matter not described in the specification. Hence, Claims 7, 24 and 37-41 are rejected for introducing new matter.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

35 USC § 112: Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 7, 24 and 37-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 24 and 37-40 are indefinite in Claim 24 for the recitation "wherein the binding agent is capable of immobilizing a probe to the biochip" because it is unclear whether a probe is immobilized. The method steps (b) and (c) do not recite probe immobilization and therefore it is unclear whether the spotting of steps (b) and (c) result in probe immobilization and/or producing a biochip comprising immobilized probes. It is suggested that Claim 24 be amended to clarify e.g. in step (c) after "thereby producing a biochip comprising a plurality of spots comprising" insert "immobilized".

Claim 41 is indefinite for the recitation "wherein the binding agent is capable of immobilizing a probe to the biochip" because it is unclear whether a probe is immobilized. The method steps (b) and (c) do not recite probe immobilization and therefore it is unclear whether the spotting of steps (b) and (c) result in probe immobilization and/or producing a biochip comprising immobilized probes. It is suggested that Claim 41 be amended to clarify e.g. in step (c) after "thereby producing a biochip comprising a plurality of spots comprising" insert "immobilized".

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 6, 23, 25, 26, 28, 29 and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by Balch (U.S. Patent No. 6,083,763, filed 31 December 1997).

Regarding Claim 6, Balch discloses the method of Claim 26 wherein the plate comprise a material selected from the group consisting of a nylon membrane, a glass and a polymer plastic (Column 9, lines 56-60)

Regarding Claim 23, Balch discloses the method of Claim 26 wherein the plate is substantially planar (Column 9, lines 56-60).

Regarding Claim 25, Balch discloses a method for producing a biochip comprising: providing a mixture of a binding agent and a probe (i.e. biotin derivatized nucleic acid and the attached probe) wherein said binding agent is capable of immobilizing a probe to the biochip having a streptaviden film; spotting the mixture to a plurality of positions on the biochip; and spotting a plurality of probes onto the positions where the binding agent is spotted thereby producing a biochip (Column 6, lines 1-24 and Column 18, lines 55-66) and wherein the mixture is spotted with a tube (Column 12, lines 12-17). The claims are broadly drawn to a method for producing a biochip comprising providing a mixture of binding agent and probe. Balch teaches a probe attached to a biotin moiety wherein the biotin functions as a binding agent to immobilize the probe to the biochip. The claims are given the broadest reasonable

interpretation consistent with the broad claim language and the specification wherein "binding agent" is not clearly define. Because Balch teaches a probe-binding agent mixture, Balch teaches the biochip as claimed.

Regarding Claim 26, Balch discloses a method for producing a biochip comprising: providing a plate (i.e. solid support); providing a mixture of a binding agent and a probe (i.e. biotin derivatized nucleic acid and the attached probe) wherein said binding agent is capable of immobilizing a probe to the biochip having a streptaviden film; spotting the mixture to a plurality of positions on the biochip; and spotting a plurality of probes onto the positions where the binding agent is spotted thereby producing a biochip (Column 6, lines 1-24 and Column 18, lines 55-66) wherein the mixture is spotted with a tube (Column 12, lines 12-17). The claims are broadly drawn to a method for producing a biochip comprising providing a mixture of binding agent and probe. Balch teaches a probe attached to a biotin moiety wherein the biotin functions as a binding agent to immobilize the probe to the biochip. The claims are given the broadest reasonable interpretation consistent with the broad claim language and the specification wherein "binding agent" is not clearly define. Because Balch teaches a probe-binding agent mixture, Balch teaches the biochip as claimed.

Regarding Claim 28, Balch discloses the method wherein the mixture is spotted with a tube (Column 12, lines 12-17).

Regarding Claim 29, Balch discloses the method wherein the tube is capillary tube (Column 12, lines 12-17).

Regarding Claim 35, Balch discloses the method of Claims 25 of 26 wherein the mixture is carried by a tip of the tube and spotted with the tube onto a plurality of positions on the biochip (Column 15, lines 10-60).

Response to Arguments

11. Applicant argues that Balch immobilizes biotin-conjugated nucleic acid to a streptavidin on the surface of the array and not the non-conjugated binding agent as instantly claimed. The argument has been considered but because the "non-conjugated binding agent" is deemed

new matter (see paragraphs 4-6 above) and arguments regarding the new matter limitations are deemed moot.

Applicant further argues that methods of Balch utilize a streptavidin film which differs from the instant invention wherein the binding agent is only provided on an area of the biochip or plate where the probe is spotted. The argument has been considered but is not found persuasive because, as stated previously and reiterated above, the binding agent of Balch is considered to be biotin. The claims are drawn to a "binding agent" the claims do not limit the binding agent to streptavidin. Therefore, Applicant's assertion that Balch does not disclose the instant invention is not relevant to the instant claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

12. Claims 6, 23, 25-27 and 30-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Martinsky (U.S. Patent No. 6,101,946, filed 13 November 1998) as taught by TeleChem International (http://www.arrayit.com//products/solutions/mss/mss.html, copyright 1998,1999).

Regarding Claim 6, Martinsky discloses the method of Claim 26 wherein the plate comprises glass i.e. microscope slide (Column 8, lines 53-55).

Regarding Claim 23, Martinsky discloses the method of Claim 26 wherein the plate is substantially planar i.e. microscope slide (Column 8, lines 53-55).

Regarding Claim 25, Martinsky discloses a method for producing a biochip comprising: providing a mixture of a binding agent (i.e. Micro-Spotting Solution) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip; and spotting the mixture to a plurality of positions on the biochip wherein the binding agent is only provided on an area of the biochip where the probe is spotted thereby producing a biochip (Column 8, lines 51-58)

wherein the mixture is spotted with a pin (Abstract) and wherein the probe binding agent is not conjugated to the probe i.e. the binding agent comprises "polymers and charged components" (Column 8,lines 55-58). Additionally, TeleCom International teaches their Micro-Spotting Solution comprises agents which stabilizes DNA spots, improves spotting consistency and improves deposition precision (see page 2, Fig. 1). As such the polymers and charged components of TeleCom facilitate spotting and stabilize DNA spots on the array.

Regarding Claim 26, Martinsky discloses a method for producing a biochip comprising: providing a plate i.e. slide); providing a mixture of a binding agent (i.e. Micro-Spotting Solution) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip; and spotting the mixture to a plurality of positions on the biochip wherein the binding agent is only provided on an area of the biochip where the probe is spotted thereby producing a biochip (Column 8, lines 51-58) wherein the mixture is spotted with a pin (Abstract).) and wherein the probe binding agent is not conjugated to the probe i.e. the binding agent comprises "polymers and charged components" (Column 8,lines 55-58). Additionally, TeleCom International teaches their Micro-Spotting Solution comprises agents which stabilizes DNA spots, improves spotting consistency and improves deposition precision (see page 2, Fig. 1). As such the polymers and charged components of TeleCom facilitate spotting and stabilize DNA spots on the array.

Regarding Claim 27, Martinsky discloses the method of Claims 25 and 26 wherein the mixture is spotted with a pin (Abstract).

Regarding Claim 30, Martinsky discloses the method of Claim 27 wherein the tip comprises at least one recess (Column 6, lines 21-57).

Regarding Claim 31, Martinsky discloses the method of Claim 30 wherein the recess comprises a concave shape (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 32, Martinsky discloses the method of Claim 31 wherein the recess comprises at least one groove i.e. gap (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 33, Martinsky discloses the method of Claim 32 wherein the groove comprises a radially-shaped groove (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 34, Martinsky discloses the method of Claims 25 and 26 wherein the mixture is suctioned (by immersing the pins in the mixture) and spotted on a plurality of positions on the biochip (Column 7, lines 66-7 and Column 8, lines 13-15).

Regarding Claim 35, Martinsky discloses the method of Claims 25 and 26 wherein the mixture is carried by a tip of a pin and spotted on a plurality of positions on the biochip (Column 8, lines 27-40).

Regarding Claim 36, Martinsky discloses the method of Claims 25 and 26 wherein the mixture is carried by surface tension by a tip of a pin and spotted on a plurality of positions on the biochip i.e. printing results from direct contact with the biochip surface (Column 8, lines 31-33) therefore, the contact breaks the surface tension between the tip and the mixture to provide printing.

Response to Arguments

13. Applicant argues that Martinsky and TeleChem do not disclose the claimed method because their binding agent is the silane coating which coats the entire surface of the slide providing a biochip comprising binding agent on portions of the slide where there is no probe. The argument has been considered but is not found persuasive because, as stated previously and reiterated above, the binding agent of Martinsky is considered to be the Micro-spotting solution of TeleChem. The claims are drawn to a "binding agent capable of immobilizing a probe to the biochip" the claims do not limit the binding agent to silane coating and the claims do not limit the immobilization to a specific type of immobilization (e.g. covalent attachment). Therefore, Applicant's assertion that Martinsky does not disclose the instant invention is not relevant to the instant claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant further argues that TeleChem does not mention binding ability and therefore does not disclose a solution comprising any binding agents. The argument has been considered but is not found persuasive because, as stated above, the claims are drawn to a

"binding agent capable of immobilizing a probe to the biochip" the claims do not limit the binding agent to silane coating and the claims do not limit the immobilization to a specific type of immobilization (e.g. covalent attachment). Therefore, Applicant's assertion that TeleChem does not disclose binding agents is not relevant to the instant claims. Additionally, TeleChem teaches that the Micro-spotting solution "improves deposition precision"; "increases deposition uniformity"; and "stabilizes DNA" all of which are encompassed by the broadly claimed "binding agent which is capable of immobilizing".

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 6, 23-31 and 34-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kang et al (U.S. Patent No. 6,268,131 B1, filed 15 December 1997).

Regarding Claim 6, Kang et al teach the plate comprises a material selected from the group consisting of glass, silicone wafer and polymer plastic (Column 7, lines 26-38).

Regarding Claim 23, Kang et al teach the plate is substantially planar (Column 7,lines 31-35).

Regarding Claim 24, Kang et al teach a method for producing a biochip comprising a plurality of spots comprising, providing a binding agent capable of immobilizing a probe to the biochip (i.e. crosslinker) and spotting the binding agent to a plurality of positions on the biochip and subsequently spotting a plurality of probes onto the positions having the binding agent wherein the probes are spotted with a pin thereby producing a biochip comprising a

plurality of spots comprising probes wherein the probe is present only at positions on the biochip wherein the binding agent is present i.e. the crosslinking agent is provided on the biochip to provide desired spacing of the immobilized nucleic acids from each other (Column 9, line 60-Column 10, line 42, especially, Column 10, lines 26-32). Kang et al do not specifically teach the crosslinking agent is spotted using a pin or tube. However, they specifically teach providing the crosslinking agent to provide spacing between immobilized nucleic acids and they teach a device for "spotting" solutions onto the biochip i.e. pin assembly (Column 17, lines 59-Column 18, line 9 and Column 19, line 51-Column 20, line 6 and Fig. 1-2). Kang et al teach applying the binding agent prior to spotting the probes and they teach the binding agent applied to provide desired spacing between probes which are spotted using spaced pins. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the spotting pin of Kang et al and to spot their crosslinker onto the biochip using their pins having the desired probe spacing to thereby efficiently spot both the crosslinker and probe with desired spacing for the obvious benefits of economy of reagents i.e. spotting the crosslinker with spacing would consume less crosslinker reagent than would be consumed by coating the biochip surface with the crosslinker.

Regarding Claim 25, Kang et al teach a method for producing a biochip comprising a plurality of spots comprising: providing a binding agent (i.e. cleavable linker) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip and the binding agent is not conjugated to the probe (i.e. the photocleavable linker is cleaved to then immobilize the probe to the biochip, Column 12, line 61-Column 13, line 17) spotting the mixture onto a plurality of positions on the surface of the biochip thereby producing a biochip comprising a plurality of immobilized spots in which the binding agent and probe are present (Column 9, line 60-Column 10, line 42, especially, Column 10, lines 26-32 and Column 13, lines 15-17). Kang et al do not specifically teach the binding agent and probe are in a mixture which is spotted as a mixture. However, it would have been obvious to one of ordinary skill in the art at

the time the claimed invention was made to mix the binding agent and probe of Kang et al and to spot the mixture onto the biochip for the obvious benefit spotting both the binding agent and probe in a single spotting step.

Regarding Claim 26, Kang et al teach a method for producing a biochip comprising a plate comprising a plurality of spots comprising: providing a plate; providing a binding agent (i.e. cleavable linker) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip and the binding agent is not conjugated to the probe (i.e. the photocleavable linker is cleaved to then immobilize the probe to the biochip, Column 12, line 61-Column 13, line 17) spotting the mixture onto a plurality of positions on the surface of the biochip thereby producing a biochip comprising a plurality of immobilized spots in which the binding agent and probe are present (Column 9, line 60-Column 10, line 42, especially, Column 10, lines 26-32 and Column 13, lines 15-17). Kang et al do not specifically teach the binding agent and probe are in a mixture which is spotted as a mixture. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to mix the binding agent and probe of Kang et al and to spot the mixture onto the biochip for the obvious benefit spotting both the binding agent and probe in a single spotting step.

Regarding Claim 27, Kang et al teach the method of Claim 25 or 26 wherein the mixture is spotted with a pin (Column 4, lines 1-3 and Fig. 2).

Regarding Claim 28, Kang et al teach the method of Claim 25 or 26 wherein the mixture is spotted with a tube (i.e. capillary/needle, Column 18, lines 59-67 and Column 20, lines 17-22).

Regarding Claim 29, Kang et al teach the method of Claim 28 wherein the tube is a capillary tube (i.e. capillary/needle, Column 18, lines 59-67 and Column 20, lines 17-22).

Regarding Claim 30, Kang et al teach the method of Claim 27 wherein the pin comprises a tip comprising at least one recess (Column 17, lines 24-28 and Column 18, lines 59-65).

Regarding Claim 31, Kang et al teach the method of Claim 30 wherein the recess comprises a concave shape (Column 17, lines 24-28).

Regarding Claim 34, Kang et al teach the method of Claim 25 or 26 wherein the solution is suctioned by the pin and spotted onto a plurality of position on the biochip (Column 18, line 59-Column 19, line 25).

Regarding Claim 35, Kang et al teach the method of Claim 25 or 26 wherein the solution is carried by a tip of the pin and spotted with the pin onto a plurality of positions on the biochip (Column 19, line 63-Column 20, line 6).

Regarding Claim 36, Kang et al teach the method of Claim 25 or 26 wherein the probe comprises a solution and the solution is carried by surface tension by a tip of the pin and spotted with the pin onto a plurality of positions on the biochip (Column 19, line 63-Column 20, line 6).

Regarding Claim 37, Kang et al teach the method of Claim 24 wherein the pin comprises a tip comprising at least one recess (Column 17, lines 24-28 and Column 18, lines 59-65).

Regarding Claim 38, Kang et al teach the method of Claim 24 wherein the probe is suctioned by the pin and spotted onto a plurality of position on the biochip (Column 18, line 59-Column 19, line 25).

Regarding Claim 39, Kang et al teach the method of Claim 24 wherein the probe is carried by a tip of the pin and spotted with the pin onto a plurality of positions on the biochip (Column 19, line 63-Column 20, line 6).

Regarding Claim 40, Kang et al teach the method of Claim 24 wherein the probe comprises a solution and the solution is carried by surface tension by a tip of the pin and

spotted with the pin onto a plurality of positions on the biochip (Column 19, line 63-Column 20, line 6).

Regarding Claim 41, Kang et al teach a method for producing a biochip comprising a plurality of spots comprising, providing a binding agent capable of immobilizing a probe to the biochip (i.e. crosslinker) and spotting the binding agent to a plurality of positions on the biochip and subsequently spotting a plurality of probes onto the positions having the binding agent wherein the probes are spotted with a pin wherein the pin comprises a tip comprising at least on recess (Column 17, lines 24-28 and Column 18, lines 59-65) thereby producing a biochip comprising a plurality of spots comprising probes wherein the probe is present only at positions on the biochip wherein the binding agent is present i.e. the crosslinking agent is provided on the biochip to provide desired spacing of the immobilized nucleic acids from each other (Column 9, line 60-Column 10, line 42, especially, Column 10, lines 26-32). Kang et al do not specifically teach the crosslinking agent is spotted using a pin or tube. However, they specifically teach providing the crosslinking agent to provide spacing between immobilized nucleic acids and they teach a device for "spotting" solutions onto the biochip i.e. pin assembly (Column 17, lines 59-Column 18, line 9 and Column 19, line 51-Column 20, line 6 and Fig. 1-2). Kang et al teach applying the binding agent prior to spotting the probes and they teach the binding agent applied to provide desired spacing between probes which are spotted using spaced pins. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the spotting pin of Kang et al and to spot their crosslinker onto the biochip using their pins having the desired probe spacing to thereby efficiently spot both the crosslinker and probe with desired spacing for the obvious benefits of economy of reagents i.e. spotting the crosslinker with spacing would consume less crosslinker reagent than would be consumed by coating the biochip surface with the crosslinker.

16. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kang et al 6,268,131 B1, filed 15 December 1997) as applied to Claims 24-26 above and further in view of Beattie (U.S. Patent No. 5,843,767, filed 10 April 1996).

Regarding Claim 7, Kang et al teach a method for producing a biochip comprising a plate comprising a plurality of spots comprising: providing a plate; providing a binding agent (i.e. cleavable linker) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip and the binding agent is not conjugated to the probe (i.e. the photocleavable linker is cleaved to then immobilize the probe to the biochip, Column 12, line 61-Column 13, line 17) spotting the mixture onto a plurality of positions on the surface of the biochip thereby producing a biochip comprising a plurality of immobilized spots in which the binding agent and probe are present (Column 9, line 60-Column 10, line 42, especially, Column 10, lines 26-32 and Column 13, lines 15-17). Kang et al teach numerous and various linkers were known and applicable to their method (Column 11, line 14-Column 13, line 44) but they do not specifically teach poly-l-lysine, carbodiimide and silylation-coating linkers. However, spotting with silylation-coating was well known in the art at the time the claimed invention was made as taught by Beattie et al (Example 4, Column 13, line 55-Column 14, line 11). Beattie et al teach a similar method of producing a biochip comprising providing a binding agent (i.e. silylation-coating) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip and the binding agent is not conjugated to the probe; spotting the agent and probe onto a plurality of positions on the surface of the biochip thereby producing a biochip comprising a plurality of immobilized spots in which the binding agent and probe are present wherein their silylation and probe spotting method produces a biochip with improved immobilization and isolation (Column 6, lines 21-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the silylation and

probe spotting of Beattie et al to the probe immobilization of Kang et al for the obvious benefits of improved immobilization and isolation as taught by Beattie et al (Column 6, lines 21-25).

17. Claims 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kang et al 6,268,131 B1, filed 15 December 1997) as applied to Claims 24-26 above and further in view of Martinsky (U.S. Patent No. 6,101,946, filed 13 November 1998).

Regarding Claims 32 and 33, Kang et al teach the pin comprises a tip comprising at least one recess wherein the recess comprises a concave shape (Column 17, lines 24-28) but they do not teach the recess comprises a groove (Claim 32) or a radially-shaped groove (Claim 33). However, Martinsky teaches a similar method comprising spotting a mixture with a pin wherein the recess comprises a radially-shaped groove i.e. gap (Column 6, lines 21-57 and Fig. 4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the pin formation of Kang et al with the radially-shaped groove of Martinsky based on desired volume, size and shape of biochip spots for the obvious benefits of optimizing spots characteristics to thereby maximize experimental results.

18. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Martinsky (U.S. Patent No. 6,101,946, filed 13 November 1998) as taught by TeleChem International (http://www.arrayit.com//products/solutions/mss/mss.html, copyright 1998,1999).

Regarding Claim 7, Martinsky teaches a method for producing a biochip comprising: providing a mixture of a binding agent (i.e. Micro-Spotting Solution) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip; and spotting the mixture to a plurality of positions on the biochip wherein the binding agent is only provided on an area of the biochip where the probe is spotted thereby producing a biochip (Column 8, lines 51-58) and a method for producing a biochip comprising: providing a plate i.e. slide); providing a mixture of a binding agent (i.e. Micro-Spotting Solution) and a probe wherein the binding agent is capable of immobilizing the probe to the biochip; and spotting the mixture to a plurality of positions on the biochip wherein the binding agent is only provided on an area of the biochip where the probe is spotted thereby producing a biochip (Column 8, lines 51-58). Additionally. Martinsky teaches an additional binding agent wherein the binding agent is silyation-coating (Column 8, lines 53-54) but they do not teach their binding agent-probe mixture comprises silyation coating. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the spotting mixture of Martinsky to include the silylated coating to thereby locally spot all binding agents in one step and eliminating the added time and expense of purchasing silylated slides for the obvious benefit of economy of time and labor.

Response to Arguments

19. Applicant argues that Martinsky and TeleChem do not teach or suggest the claimed invention because as argued above, Martinsky does not disclose the claimed method because their binding agent is the silane coating which coats the entire surface of the slide providing a biochip comprising binding agent on portions of the slide where there is no probe. The argument has been considered but is not found persuasive for the reasons stated above i.e. the claims are drawn to a "binding agent capable of immobilizing a probe to the biochip" the claims do not limit the binding agent to silane coating and the claims do not limit the immobilization to a specific type of immobilization (e.g. covalent attachment). Therefore, Applicant's assertion that Martinsky and TeleChem do not teach or suggest the instant invention is not relevant to the instant claims.

20. Claims 21, 24 and 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinsky (U.S. Patent No. 6,101,946, filed 13 November 1998) as taught by TeleChem International (http://www.arrayit.com//products/solutions/mss/mss.html, copyright 1998,1999) in view of Beattie (U.S. Patent No. 5,843,767, issued 1 December 1998).

Regarding Claim 21, Martinsky teaches the method wherein the pin comprises at least one recessed tip (Column 4, lines 24-34 and Fig. 3 B and 4).

Regarding Claim 24, Martinsky teaches a method for producing a biochip comprising: providing a binding agent (i.e. Micro-Spotting Solution) wherein the binding agent is capable of immobilizing the probe to the biochip and a probe; spotting the binding agent to a plurality of positions on the biochip and spotting a plurality of probes onto the positions having the binding agent wherein the binding agent is only provided on an area of the biochip where the probe is spotted thereby producing a biochip (Column 8, lines 51-58). Additionally, TeleCom International teaches their Micro-Spotting Solution comprises binding agents capable of immobilizing the probe to the biochip (see page 2, Fig. 1). Martinsky does not teach the binding agent is spotted prior to the step of spotting the probes. However, Beattie et al. teach a similar method wherein a binding agent is spotted onto the biochip prior to spotting the probe wherein their method provides an improved biochip having a high density of probes fixed in isolated a discrete regions (Column 6, lines 7-13 and 21-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the spotting steps of Martinsky and to spot a binding agent onto the biochip prior to spotting the probe to thereby provide an high density of probes in discrete and isolated regions for the expected benefit of providing a biochip capable of conducting a multiplicity of individual and simultaneous binding reactions as taught by Beattie et al. (Abstract).

Regarding Claim 30, Martinsky teaches the method wherein the tip comprises at least one recess (Column 6, lines 21-57).

Regarding Claim 31, Martinsky teaches the method wherein the recess comprises a concave shape (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 32, Martinsky teaches the method wherein the recess comprises at least one groove i.e. gap (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 33, Martinsky teaches the method wherein the groove comprises a radially-shaped groove (Column 6, lines 21-57 and Fig. 4).

Regarding Claim 34, Martinsky teaches the method wherein the mixture is suctioned (by immersing the pins in the mixture) and spotted on a plurality of positions on the biochip (Column 7, lines 66-7 and Column 8, lines 13-15).

Regarding Claim 35, Martinsky teaches the method wherein the mixture is carried by a tip of a pin and spotted on a plurality of positions on the biochip (Column 8, lines 27-40).

Regarding Claim 36, Martinsky teaches the method wherein the mixture is carried by surface tension by a tip of a pin and spotted on a plurality of positions on the biochip i.e. printing results from direct contact with the biochip surface (Column 8, lines 31-33) therefore, the contact breaks the surface tension between the tip and the mixture to provide printing.

Response to Arguments

21. Applicant argues that Martinsky does not teach a binding agent is spotted prior to spotting the probes and because the binding agent of Martinsky is the silane coating, the binding agent is on portions where there is no probe. The argument has been considered but is not found persuasive for the reasons stated above i.e. the claims are drawn to a "binding agent capable of immobilizing a probe to the biochip". The claims are not limited to a silane binding agent and the claims are not limited to a specific type of immobilization (e.g. covalent attachment). Therefore, Applicant's assertion that Martinsky does not disclose the instant invention is not relevant to the instant claims.

Applicant further argues that TeleChem does not teach a solution comprising a binding agent is spotted prior to the probe. Applicant further argues that Beattie fails to cure the deficiencies of Martinsky and TeleChem because Beattie does not teach "spotting". In

response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Beattie and Martinsky/TeleChem teach different methods for producing a biochip. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of skill in the art would have been motivated to apply the silylation and probe spotting of Beattie et al to the probe immobilization of Martinsky for the obvious benefits of improved immobilization and isolation as taught by Beattie et al (Column 6, lines 21-25).

22. Claims 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinsky (U.S. Patent No. 6,101,946, filed 13 November 1998) as taught by TeleChem International (http://www.arrayit.com//products/solutions/mss/mss.html, copyright 1998,1999) in view of Beattie (U.S. Patent No. 5,843,767, issued 1 December 1998) as applied to Claim 24 above and further in view of Balch (U.S. Patent No. 6,083,763, filed 31 December 1997).

Regarding Claims 28 and 29, Martinsky teaches a method for producing a biochip comprising: providing a binding agent (i.e. Micro-Spotting Solution) wherein the binding agent is capable of immobilizing the probe to the biochip and a probe; spotting the binding agent to a plurality of positions on the biochip and spotting a plurality of probes onto the positions having the binding agent wherein the binding agent is only provided on an area of the biochip where

the probe is spotted thereby producing a biochip (Column 8, lines 51-58). Additionally, TeleCom International teaches their Micro-Spotting Solution comprises binding agents capable of immobilizing the probe to the biochip (see page 2, Fig. 1). Martinsky does not teach the binding agent is spotted prior to the step of spotting the probes. However, Beattie et al. teach a similar method wherein a binding agent is spotted onto the biochip prior to spotting the probe wherein their method provides an improved biochip having a high density of probes fixed in isolated a discrete regions (Column 6, lines 7-13 and 21-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the spotting steps of Martinsky and to spot a binding agent onto the biochip prior to spotting the probe to thereby provide an high density of probes in discrete and isolated regions for the expected benefit of providing a biochip capable of conducting a multiplicity of individual and simultaneous binding reactions as taught by Beattie et al. (Abstract). Martinsky and Beattie et al. do not teach the method wherein the probe or binding agent is spotted with a pin. However, Balch teaches as similar method for producing a biochip comprising: spotting a binding agent and a plurality of probes onto a biochip wherein said binding agent is capable of immobilizing a probe to the biochip (Column 6, lines 1-24 and Column 18, lines 55-66) wherein the binding agent and probe are spotted with a capillary tube whereby capillary spotting permits small volume spotting with minimal evaporation or cross contamination (Column 12, lines 13-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the pin spotting of Martinsky and Beattie et al. with the capillary tube spotting as taught by Balch to thereby minimize evaporation and cross contamination for the expected benefit of efficient and accurate spotting as taught by Balch (Column 12, lines 30-35).

Response to Arguments

23. Applicant argues that Martinsky and TeleChem and/or Beattie and/or Balch do not teach or suggest the instant invention as argued above. The arguments are not found persuasive as discussed above in paragraphs 11, 13, 19 and 21.

Conclusion

24. No claim is allowed.

25. The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
August 7, 2002